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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,322	09/12/2006	Birgit Baumgarten	4-33201A	4964

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

NOTIFICATION DATE	DELIVERY MODE
10/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,322	BAUMGARTEN ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7 and 10-18* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 10-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's amendment filed on 08/16/2010 has been entered. Claim 7 is amended. Claims 5-7 and 10-18 are pending. Claims 7 and 16-18 are under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 7 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for a candidate compound that antagonizes or agonizes a GPR4 related polypeptide comprising the amino acid sequence of SEQ ID NO: 3, does not reasonably provide enablement for a method for screening for a candidate compound that antagonizes or agonizes a GPR4 related polypeptide comprising an amino acid sequence that is at least 95% identical the amino acid sequence of SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is maintained for the reasons set forth in the office action mailed on 04/16/2010.

Applicants argue that the claims require that the recited polypeptides comprises at least 95% sequence identity to the sequence of SEQ ID NO: 3. Applicants argue that the specification clearly identifies human GPR4 polypeptide as a member of the G-protein coupled receptor family. Applicants argue that there was considerable knowledge and sufficient guidance in the art which would direct one of skill to the portions and structural features of GPR4 which might be critical for activity. Applicants argue that newly amended claim 7 includes a functional limitation whereby a GPR4 related polypeptide with at least 95% sequence identity to SEQ ID NO: 3 activates cAMP formation in response to pH conditions that stimulate GPR4. Applicants argue that the specification clearly discloses a cAMP formation assay which could easily be used by one of skill in the art to measure the function of GPR4 and GPR4-related polypeptides with at least 95% identity to SEQ ID NO: 3 and determine which polypeptides with 95% identity to SEQ ID NO: 3 were operable and retained the recited function of a GPR4-related polypeptide.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the 95% identity to the amino acid sequence of SEQ ID NO: 3 does not represent a conserved structure because it says nothing about the amino acid residues that are critical for the functional activity of the GPR4 polypeptide. While GPR4 belongs to the a family of GPCR, such a assignment does not provide readily and direct guidance with respect to how to determine the conserved structure that is critical for the activity of the GPR4 polypetide because GPCR family members have a

diversified structural and biological activities even though they share seven transmembrane domains.

Secondly, the method of screening for a GPR4 polypeptide that retains the biological function is not equivalent to a method of making a GPR4 polypeptide. The specification does not provide sufficient guidance/direction or working examples on the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. There are no working examples of using polypeptides that are less than 100% identical to the polypeptide SEQ ID NO: 3. The instant disclosure does not show (i) which portions of the human GPR4 polypeptide of SEQ ID NO: 3 are critical to its activity; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 3 will result in a mutant or a fragment with the same functions as the polypeptide set forth in SEQ ID NO: 3. It is unpredictable whether a variant or homologue of SEQ ID NO: 3 would retain the same function as that of the full length of polypeptide of SEQ ID NO: 3. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein. The prior art teaches a human GPR4 polypeptide (see, e.g., Mahadevan et al., Genomics 30:84-88, 1995; Yang et al., US Patent No. 6,919,176 B2). However, the

prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to make and use *the recited genus* of polypeptides in the claimed methods. In this respect, it is noted that the specification discloses that SPC, which is reported to be a ligand for GPR4, does not modulate pH-dependent stimulation and does not activate cAMP formation on its own (page 41, the 2nd paragraph of the specification). Thus, in view of the nature of complexity of the work and unpredictability of the art, it would take undue experimentation for one skilled in the art to make and use the claimed methods of polypeptides without sufficient guidance, working examples, and knowledge about functions of encompassed polypeptides structurally related to SEQ ID NO: 3.

Accordingly, while being enabling for a method for screening for an agonist or antagonist of a human GPR4 polypeptide comprising the amino acid sequence of SEQ ID NO: 3, does not reasonably provide enablement for a method for screening for a candidate compound that antagonizes or agonizes a GPR4 related polypeptide comprising an amino acid sequence that is at least 95% identical the amino acid sequence of SEQ ID NO: 3.

(ii). Claims 7 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Amended claim 7 is drawn to a method for screening for an agonist or antagonist of a GPR4 related polypeptide comprising a polypeptide having at least 95% identity to the polypeptide sequence of SEQ ID NO: 3 and activated cAMP formation in response to pH conditions that stimulate GPR4. The claim is broad because it encompasses a broad genus of GPR4 variants and homologues without reciting any particular conserved structure. Claims 16-18 depend from claim 7.

The instant disclosure of human GPR4 polypeptide of SEQ ID NO: 3 does not adequately support the scope of the recited genus, which encompasses a substantial variety of human GPR4 homologues or variants. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case, the specification merely

discloses a single GPR4 polypeptide, which is not sufficient to support the broad genus encompassed in the instant claims. Moreover, while disclosing human GPR4 polypeptides of SEQ ID NO: 3, the instant disclosure fails to provide sufficient description information, such as definitive structural features of the recited genus of human GPR4 variants and homologues. There is no description of the conserved regions that are critical to the function of the genus of human GPR4 variants and homologues. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function.

The prior art teaches a human GPR4 polypeptide (see, e.g., Mahadevan et al., Genomics 30:84-88, 1995; Yang et al., US Patent No. 6,919,176 B2). However, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed genus of human GPR4 variants and homologues.

Accordingly, due to the breadth of the recited genus of GPR4 variants and homologues and lack of the definitive structural features of the recited genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the recited genus of the human GPR4 variants and homologues.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
September 29, 2010